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Hb Crete in a Turkish Family with Crete Island origin

Duran Canatan[1,4], İbrahim Keser[2], Türker Bilgen[3], and Serpil Delibaş[4]

[1]Antalya Genetic Diagnostic Center – Antalya, Turkey
[2]Akdeniz University Medical Faculty, Department of Biology and Genetics – Antalya, Turkey
[3]Research and Application Centre for Scientific and Technological Investigations (NABILTEM) of Namik Kemal University- Tekirdağ, Turkey
[4]Hemoglobinopathy Diagnostic Center of Mediterranean Blood Diseases Foundation- Antalya, Turkey

Abstract

Hemoglobin Crete is an abnormal hemoglobin of beta chain with high oxygen affinity and neutral and unstable as electrophoretic. It is characterized by erytrocytosis and microcytosis as clinically and [beta129(H7)Ala>Pro] as molecularly. First time, it was reported a combination of beta and delta-beta mutations and also in a homozygous state in a Greek family emigrated to the United States from the island of Crete. Here in first time, we report a Turkish family with Hb Crete and thalassemic mutation IVS1.110 (G> A).

Introduction

Hemoglobin Crete is an abnormal hemoglobin of beta chain with high oxygen affinity and neutral as electrophoretic. The erytrocytosis and microcytosis is remarkable as clinically. It is characterized by Ala> Pro in beta chain [beta129 (H7) Ala>Pro] [1]. First time, it was reported a combination of beta and delta-beta mutations and also in a homozygous state in a Greek family emigrated to the United States from the island of Crete [2,3]. In our country, first case who emigrated from the island of Crete to Turkey was reported by Arslan *et al.* [4]. We report a family with Hb Crete and thalassemic mutation IVS1.110 (G> A) in our country.

Case

A seventeen-year-old female patient was admitted to our center with complaints with paleness and weakness. We learned that the origin of the family emigrated to Antalya from the Crete island five generations ago. In the physical examination, she had pallor, the scar of cholecystectomy and splenomegaly. Her complete blood count (CBC) was microcytosis, hypochromia, erythrocytosis, and anizositosis in Table 1. The result of High Performance Liquid Chromatography (HPLC) showed 90% HbA1, 5.7%, HbA 2 and 4.2% HbF. Mother and father was examined , her mother had also microcytosis and erythrocytosis 96%HbA1 3.4% HbA2 and 1% HbF in HPLC, while the father had mild anemia and microcytosis besides of 93% HbA1 and 6.4% HbA2 was found in HPLC (Table 1 and 2) . We have informed constent for analysis DNA sequencing analysis. Following DNA extraction by a commercial kit (Roche, Mannheim, Germany) and amplification of the whole beta globin gene by standard protocols of PCR and DNA sequencing (Applied Biosystems, USA). We found compound heterozygous for Hb Crete (HBB:c.388 G>C) and IVS.1.110 (G>A) in case. (Figure 1) Her mother was the trait of Hb Crete (HBB:c.388 G>C) and her father was the trait of IVS1.110 (G>A) (Table2)

Discussion

Although hematological and HPLC results are normal level in Hb Crete carriers , a definitive diagnosis is established by DNA analysis, but sometimes clinically may be change in association with severe beta-thalassemia mutations. First identified case had hemolysis, erythrocytosis, abnormal red cell morphology, splenomegaly and marked erythroid hyperplasia symptoms was diagnosed Hb Crete/delta beta^0 thalassemia compound heterozygous (67% Hb Crete and 30% Hb F), his father was Hb Crete/B^0 compound heterozygous thalassemia Hb Crete (84%, 5% and Hb A2 HBF 10%), and his brother was Hb Crete trait (Hb Crete 38%, 56% Hb A). (2) Two homozygous Hb Crete cases were defined in Greece and in both cases had erythrocytosis, microcytosis and mild microcytic anemia [3]. The Turkish first case had hepatosplenomegaly, extramedullary hemaotopoesis ,erythrocytosis and microcytosis . HPLC showed abnormal band (%56.9) and Hb Crete was detected in the sequence analysis of the patient [4].

We thought that our case was not an ordinary thalassemia trait, because of she had splenomegaly and cholelithiasis, microcytosis and erythrocytosis in peripheric blood and had 90% HbA1, 5.7% HbA 2 and 4.2% HbF in HPLC. Mother and father was examined , her mother had also microcytosis and erythrocytosis besides of 96%HbA1 3.4% HbA2 and 1% HbF in HPLC, while the father had mild anemia and microcytosis besides of 93% HbA1 and 6.4% HbA2 was found in HPLC. Complete sequence analysis of the beta globin gene of case was revealed compound heterozygous for Hb Crete/IVS1.110, her mother had Hb Crete and her father had IVS.1.110 G>A .

It has been shown by functional studies that Hb Crete is one of the causes of secondary erythrocytosis by increased erythropoietin levels [2]. Our index case and her mother carrier for Hb crete had mild erythrocytosis. We didn't study fonctional test.

In conclusion; sometimes Hb Crete and similar abnormal hemoglobins may not be shown by HPLC, therefore the identification

Correspondence to: HProf. Dr. Duran Canatan ,Antalya Genetic Diagnostic Center, Arapsuyu Mh 600 Sk 39/1, 07070 Konyaaltı-Antalya-Turkey, E-mail: durancanatan@gmail.com

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Table 1. The results of complete blood count in a turkish family.

	Hb (g/dl)	Hct (%)	RBC (10^{12}/l)	MCV (fl)	MCH (p/g)	MCHC (g/dl	RDW (%)	Rtc (%)	WBC (10^9/l)	PLT (10^9/l)
Case	12.2	39.8	7.12	53	16.1	31.0	17.7	1.2	8.2	207
Mother	14.0	43.5	6.57	66	21.2	32.1	18.9	1.1	7.98	269
Father	12.7	41	6.73	61	18.8	30.9	17.9	1.2	9.90	298

Table 2. The results of HPLC and DNA sequence analysis of beta gene in a turkish family.

	HbA (%)	HbA2 (%)	Hb F (%)	Anormal Hb (%)	DNA sequence analysis of beta gene
Case	90.1	5.7	4.2	0	Hb Crete / IVS1.110
Mother	96.5	3.4	1.0	0	Hb Crete / Normal
Father	92.8	6.4	0.8	0	IVS1.110 / Normal

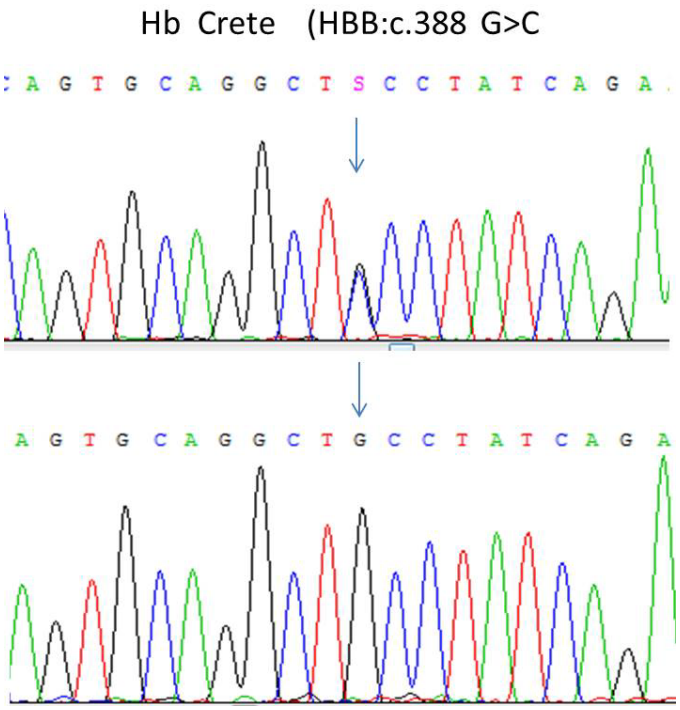

Figure 1. Hb Crete (HBB:c.388 G>C) in Beta sequence analysis.

of their needs with sequence analysis because it is a great importance in prenatal diagnosis, genetic counseling and clinical follow-up.

Conflict of interest statement

The authors of this paper have no conflicts of interest, including specific financial interests, relationships, and/or affiliations relevant to the subject matter or materials included.

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